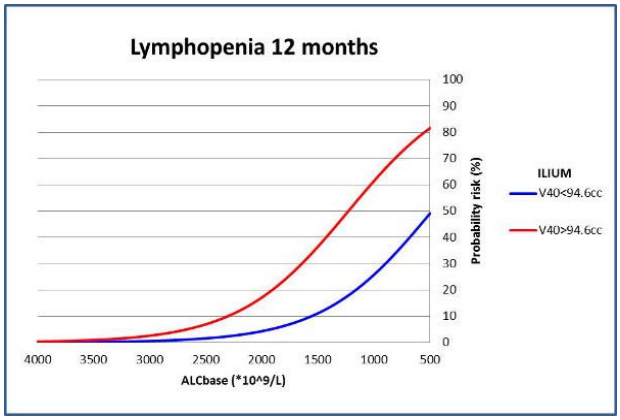
glands were independently associated with Xer_{6m}, with a correlation coefficient of 0.454 between the model predictions and Xer_{6m}. No multivariable model with multiple significant independent predictors was found for Xer_{12wk}.
A significant correlation between Xer_{6m} and Xer_{12wk} was found with a correlation coefficient of 0.627
Conclusions: The volume and density of the parotid glands and the density of the submandibular glands are associated with xerostomia after radiotherapy. The changes of these CT image features over the course of treatment are more strongly related to xerostomia than the instantaneous feature values at baseline. Moreover, the feature changes in the first 12 weeks after start of treatment are equally or even more strongly related to xerostomia at 6 month than at 12 weeks. These associations suggest that, even early after treatment, the CT image feature changes may be used as objective biomarkers of the development of xerostomia.

PD-0530

Predictors of hematological toxicity after whole-pelvis intensity-modulated post-prostatectomy radiotherapy

C. Sini[1], C. Fiorino[1], B. Noris Chiorda[2], A. Chiara[2], C. Deantoni[2], C. Gumina[2], L. Perna[1], A. Sbalchiero[2], R. Calandrino[1], N. Di Muzio[2], C. Cozzarini[2]
[1]San Raffaele Scientific Institute, Medical Physics Department, Milan, Italy
[2]San Raffaele Scientific Institute, Radiotherapy Department, Milan, Italy

Purpose/Objective: Hematologic toxicity (HT) is an important side-effect of whole pelvis intensity-modulated radiotherapy (WP-IMRT), but association between radiation dose and HT remains unclear when concurrent chemotherapy is not prescribed. The aim of this study was to identify clinical and dosimetric predictors of HT in a cohort of chemo-naïf patients treated with WPRT.
Materials and Methods: The first 121 patients enrolled in a prospective observational study, treated with adjuvant (n=72) or salvage (n=49) WP-IMRT in a single Institute were available (static field IMRT: 19; VMAT/Rapidarc:57; Helical Tomotherapy:45). Pelvic bones, used as a surrogate for pelvic bone marrow (BM), were contoured according to Mell et al [IJROBP 2006] and divided in four subvolumes: ilium (IL), lumbosacral spine (LS), lower pelvis (LP) and whole pelvis (WP). The volume of each BM region receiving 3, 5, 10, 20, 30, 40 and 50 Gy (V3-50) was recovered. Absolute values of lymphocytes (ALC), white blood cell (WBC) and neutrophils (N) were prospectively collected before WPRT, at half WPRT, at end WPRT, at 3m and at 12 months after WPRT. HT was graded according to CTCAE v. 3.0: Grade 3 (G3) and Grade 1 (G1) events were considered as end-points for acute (nadir value) and late HT respectively. Uni- and backward multi-variable logistic regression was performed to assess correlation between clinical/DVH parameters and HT. A previously introduced method based on DVH differences between patients with/without HT was used to select the most discriminative DVH parameters.
Results: The nadir of WBC and N (median values= 65% and 74% of baseline respectively) was found at half-therapy while it was at the end of RT for ALC (median= 30% of baseline). No patients showed acute G3 neither late G1 WBC and N toxicities. Interestingly, the mean value of ALC at 1 year was 54% of baseline: 28 acute G3 and 14 late G1 lymphopenias were found. Then, the analysis was restricted to ALC at the end of therapy (ALCend) and at 12 months (ALC12m). At univariate analysis, a lower baseline ALC (ALCbase) was correlated with G3 ALCend and G1 ALC12m (p=0.003 and p<0.001, respectively). Concerning dosimetric parameters, IL-V30/IL-V40 and WP-V40 were correlated with acute G3 ALCend and late G1 ALC12m (p=0.003). The resulting model for ALCend included ALCbase and WP-V40 (AUC =0.73); the model for ALC12m included ALCbase and IL-V40 (AUC= 0.82). Best cut-off values (assessed by ROC) discriminating patients with/without lymphopenia were: ALCbase ≤1830 x 10(9)/L and WP-V40 >599.4 cc (G3 ALCend); ALCbase ≤1780 x 10(9)/L and IL-V40>94.6 cc (G1 ALC12m) (Fig-1).



Conclusions: Two-variable models including ALCbase and DVH parameters of pelvic BM may predict acute G3 and late G1 lymphopenia after WP-IMRT in post-prostatectomy RT. The model could be used to reduce HT by constraining BM. Further validation on a larger population is ongoing.

PD-0531

Dosimetric investigation of rotational setup errors for spine stereotactic radiosurgery: a phantom study

M. Sasaki[1], M. Nakamura[2], N. Mukumoto[2], M. Nakata[1], K. Higashimura[1], M. Hiraoka[2]
[1]Kyoto University Hospital, Clinical Radiology Service, Kyoto, Japan
[2]Kyoto University Graduate School of Medicine, Radiation Oncology and Image-applied Therapy, Kyoto, Japan

Purpose/Objective: A final accuracy of positioning < 2 mm is the recommended tolerance level for image-guided radiotherapy (IGRT) for spine stereotactic radiosurgery (SRS) in RTOG 0631. However, the tolerance level for rotation is not specified. This study investigated experimentally the effect of rotational setup errors on dose distribution for spine SRS.
Materials and Methods: The contour definitions and treatment planning were as per RTOG 0631. A 16-Gy dose was prescribed in a single fraction by step-and-shoot intensity-modulated radiation therapy (IMRT) using seven coplanar beams with the Vero4DRT (Mitsubishi Heavy Industries, Ltd., Hiroshima, Japan, and Brainlab AG, Feldkirchen, Germany). An isocenter was placed inside the vertebral body. Setup error patterns were categorized into three groups. Only translational errors were generated for Group A, with the translational errors measuring +1, +2, +3, and +5 mm in the lateral (LAT), longitudinal (LNG), and vertical (VRT) directions, respectively. Only rotational errors were generated for Group B, and measured +1°, +2°, +3°, and +5° in terms of the tilt or roll angle. Combinations of translational and rotational errors occurred in Group C. Translational errors of 0 to 2 mm were generated in each direction and rotational errors of ±1° or ±2° in each direction. Data were acquired with a Delta4 phantom (ScandiDos, Uppsala, Sweden) and setup errors were generated with HexaMotion (ScandiDos, Uppsala, Sweden).

All measured values were evaluated using the gamma index with dose difference/distance-to-agreement criteria of 3%/2 mm ($\gamma_{3\%/2\ mm}$) for the area receiving more than 10% isodose as compared with a static pattern. A γ passing rate > 90% was considered acceptable in this study.

Results: For Group A, $\gamma_{3\%/2\ mm}$ was less than 90% for translational errors ≥ 3 mm in the LAT and VRT directions and ≥ 2 mm in the LNG direction. For Group B, $\gamma_{3\%/2\ mm}$ was less than 90% for rotational errors ≥ 3° (Table 1). Table 2 summarizes $\gamma_{3\%/2\ mm}$ for Group C. Translational errors of 2 mm and rotational errors of 2° always gave a $\gamma_{3\%/2\ mm}$ of less than 90%. $\gamma_{3\%/2\ mm}$ was less than 90% for tilt and roll angles of 2°, even without translational errors. Even when translational errors were 1 mm, $\gamma_{3\%/2\ mm}$ was less than 90% for two patterns with rotational errors of 1°. By correcting the translational errors, $\gamma_{3\%/2\ mm}$ was more than 90% for tilt and roll angles of 1°. Note that correction of the translational errors degraded $\gamma_{3\%/2\ mm}$ for the pattern with a tilt angle of 1° and roll angle of -1° and with a tile angle of 2° and roll angle of -2°.

Table 1. $\gamma_{3\%/2\ mm}$ for Group A and Group B.

Group A				Group B		
Translational error (mm)	γ3%/2 mm (%)			Rotational error (°)	γ3%/2 mm (%)	
	LAT	LNG	VRT		Tilt	Roll
1	99.4	96.5	100.0	1	99.3	97.4
2	93.7	85.6	98.2	2	92.8	92.5
3	83.7	76.2	88.6	3	83.5	87.7
5	59.5	56.7	66.5	5	73.5	72.1

Table 2. $\gamma_{3\%/2\ mm}$ for Group C.

setup error					γ3%/2 mm
LAT (mm)	LNG (mm)	VRT (mm)	Tilt (°)	Roll (°)	(%)
2	2	2	2	2	62.5
2	2	2	2	-2	84.1
2	2	2	-2	2	49.4
2	2	2	-2	-2	58.6
1	1	1	1	1	93.2
1	1	1	1	-1	96.8
1	1	1	-1	1	76.4
1	1	1	-1	-1	80.8
0	0	0	2	2	79.9
0	0	0	2	-2	73.8
0	0	0	-2	2	83.3
0	0	0	-2	-2	79.5
0	0	0	1	1	94.8
0	0	0	1	-1	94.2
0	0	0	-1	1	96.1
0	0	0	-1	-1	96.3

Conclusions: This study have demonstrated that rotational errors ≥ 3° in either angle or ≥ 1° in multiple angles most likely gave a $\gamma_{3\%/2\ mm}$ of less than 90%, even with translational errors < 2 mm; therefore, it is preferable to correct rotational errors < 2° in each angle for spine SRS under correction of translational errors.

Symposium with Proffered Papers: Future directions for HPV negative head and neck cancer

SP-0532

Molecular imaging of proliferation and hypoxia

J.H. Kaanders[1], B.A. Hoeben[1], J. Bussink[1], W.J. Oyen[2]
[1]*Radboud University Medical Center, Radiation Oncology, Nijmegen, The Netherlands*
[2]*Radboud Unicersity Medical Center, Medical Imaging, Nijmegen, The Netherlands*

HPV-status has been recognized as the strongest prognostic indicator for treatment outcome of oropharynx cancer overpowering clinical and other biological tumor characteristics. Nevertheless, the latter remain of value for selection of subgroups within the HPV-negative and HPV-positive entities that qualify for treatment intensification or de-intensification, respectively. Among the clinical factors are smoking habits and T- and N-stage. Classical radio- and chemotherapy resistance mechanisms include DNA-repair capacity, tumor repopulation and hypoxia, for which various biomarkers have been identified. To improve the outcome of HPV-negative patients the challenge is to identify the pivotal resistance mechanisms and apposite treatments to counteract them. There will not be a "one-size-fits-all" solution and customized treatment additions and/or adaptations will be essential, necessitating selection tools.

For a biomarker assay to be successful for wide clinical application it should preferably be non-invasive, fast, not too complex, and suited for repetitive assessments. PET-scanning meets these criteria although specific tracer availability can be a limitation. The current status and future directions of PET-scanning with proliferation- and hypoxia-specific tracers for outcome prediction and early response assessment will be discussed.

SP-0533

Combined modality treatment: risk-adapted intensified strategies and quality of life

C. Nutting[1]
[1]*The Royal Marsden NHS Foundation Trust, Radiotherapy, London, United Kingdom*

HPV negative head and neck cancer remains a challenging disease with a poor prognosis for many patients, especially those with locally advanced disease stage. Future developments are likely to focus on a number of areas.

Techniques to identify and target patients with radioresistant disease are required. Current clinical trials in this area are testing radiation dose escalation to overcome radioresistance. Advances in functional imaging have allowed the detection of sub-volumes of radioresistant tumour tissue due to hypoxia, proliferation or other processes. Dose painting techniques are in development to attempt to deliver increased radiatin dose to these areas.

In parallel the development of combinations of radiation with chemotherapy and novel agents are underway. The ability of agents to overcome the processes leading to radioresistance such as hypoxia, DNA damage repair and other processes will be discussed.

OC-0534

An RCT on the value of postoperative accelerated radiotherapy in squamous cell head and neck cancer: final results

J.A. Langendijk[1], J.H. Kaanders[2], P. Doornaert[3], P.L.A. Van den Ende[4], S.B. Oei[5], S. Nuyts[6], C.R. Leemans[7], H. Van Tinteren[8]
[1]*University Medical Center Groningen University of Groningen, Radiation Oncology, Groningen, The Netherlands*
[2]*Radboud University Nijmegen Medical Centre, Radiation Oncology, Nijmegen, The Netherlands*
[3]*VU University Medical Center, Radiation Oncology, Amsterdam, The Netherlands*
[4]*MAASTRO, Radiation Oncology, Maastricht, The Netherlands*
[5]*Dr. Bernard Verbeeten Instituut, Radiation Oncology, Tilburg, The Netherlands*
[6]*University Hospitals Leuven, Radiation Oncology, Leuven, Belgium*
[7]*VU University Medical Center, Otolaryngology/Head and Neck Surgery, Amsterdam, The Netherlands*
[8]*The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Medical Statistics, Amsterdam, The Netherlands*

Purpose/Objective: In head and neck squamous cell carcinoma (HNSCC), the overall treatment time of radiation (OTT) is significantly associated with locoregional control (LRC), which is consistent with rapid repopulation of cancer clonogens during radiotherapy. However, the importance of